REMARKS

I. Introduction

In response to the Office Action dated April 14, 2004, claims 34, 38, 40-42, 49 and 50 have been canceled, and claims 31, 36, 37, 39, 44, 45, 47 and 48 have been amended. Claims 31, 33, 37, 39, and 43-48 are pending. Claims 34, 36-45 and 47-50 have been withdrawn by the Examiner as directed to a non-elected invention. Claims 31 and 46 are currently being examined. Reconsideration of the application, as amended, is requested.

II. Claim Amendments

Applicants' attorney has amended claims 31, 37 and 39 to delete reference to non-elected subject matter. Claims 36, 37, 39, 44, 45, 47 and 48 have been amended to update the references to previous claims in view of the cancellation of claims 34 and 41. These amendments are made solely for the purpose of deleting non-elected subject matter and not for reasons related to patentability. Entry of these amendments is respectfully requested.

III. Restriction Requirement

Applicants acknowledge the finality of the restriction requirement, but continue to note that the Patent Office has not provided a basis for asserting that the claims are not linked by a common inventive concept. Applicants urge the Examiner to reconsider the restriction requirement and rejoin the withdrawn claims.

In particular, Applicants assert there is no basis for excluding claim 43 from the current examination directed to claims 31 and 46. In addition, Applicants have amended claims 36, 37, 39, 44, 45, 47 and 48 to make them depend on elected claim 31.

IV. Prior Art Rejections

In paragraphs (5)-(8) of the Office Action, claims 31 and 46 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Flynn et al., Biochemistry 1996, Vol. 35, pages 7308-7315 (Flynn) and Billing-Medel et al., U.S. Patent No. 6,183,952 (Billing).

Applicants respectfully traverses this rejection.

Both claims 31 and 46 (and all of the remaining claims) recite a synthetic oligonucleotide of at least 26 nucleotides in length and comprising a 5mCpG dinucleotide, wherein the 5mC is a C-5 methylcytosine, and wherein the synthetic oligonucleotide comprises a phosphorothioate nucleotide.

The cited references do not teach or suggest a synthetic oligonucleotide that comprises a phosphorothioate nucleotide. No motivation is provided in the art to modify the synthetic oligonucleotides of Flynn 1996 to arrive at the claimed subject matter.

The Examiner bases this rejection on two assertions. First, the Examiner asserts that it would have been obvious to add a pharmaceutically acceptable carrier to the GC-box b^{mer} of Flynn because the oligonucleotides of Flynn were designed to mimic DNA transcriptional elements previously reported to have cytosine C-5 methylated regulation. Second, the Examiner asserts that it would have been obvious to employ phosphorothioate internucleotide linkages in the oligonucleotide of Flynn because Billing teaches that antisense oligonucleotides act with greater efficacy when modified to contain phosphorothioate internucleotide linkages. Both of these assertions are based on erroneous assumptions.

First, Flynn describes the oligonucleotides disclosed therein as substrates for studies of DNA cytosine C-5 methyltransferase (DCMTase). The portion of Flynn (the abstract) cited by the Examiner to indicate that these substrates were designed to mimic elements "reported to have cytosine C-5-methylated regulation" merely refers to the fact that these oligonucleotides are capable of being regulated by methylation via DCMTase. This teaching does not provide a motivation for either using these substrates in a pharmaceutical composition or for introducing phosphorothioate linkages. The Flynn 1996 reference does not teach that GC-box b^{mer} regulates or modifies the activity of DCMTase. Rather, the Flynn 1996 describes the discrimination of DCMTase for various substrates (see page 7314).

Second, Billing teaches that antisense oligonucleotides act with greater efficacy when modified to contain artificial internucleotide linkages. As discussed in the same paragraph of Billing, antisense technology is used to prevent transcription and production of a targeted polypeptide (in this case, BU101). There is no teaching in the prior art, however, to use GC-box b^{mer} in the context of antisense technology to prevent transcription and production of a particular polypeptide.

Prior to the disclosure of Applicants' specification, it was not known or suggested that either GC-box b^{mer} or GC-box p^{mer} could be used as a potent inhibitor of mammalian DCMTase. Without

this information, GC-box b^{mut} was merely a substrate for the enzyme, useful in studies of enzyme mechanism and kinetics.

Thus, Applicants submit that claims 31 and 46, as well as the remaining claims, are allowable over Flynn and Billing, and withdrawal of the rejections based on the prior art is respectfully requested.

V. Conclusion

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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